ESTIMATION OF COHERENCE BETWEEN THE PULSATILE AORTIC BLOOD PRESSURE AND THE RENAL CORTICAL FLUX IN DODS

M. Y. Jan[1,3], J. J. Shyu[2], P. T. Chao[1,3], Y. Y. Lin Wang[4], W. K. Wang[1,3,*]
[1]Biophysic Lab., Institute of Physics, Academia Sinica, Taipei, Taiwan, R.O.C.
[2]Department of Veterinary Medicine, National Taiwan University, Taipei, Taiwan, R.O.C.
[3] Department of Electric Engineering, National Taiwan University, Taipei, Taiwan, R.O.C.
[4]Department of Physics, National Taiwan Normal University, Taipei, Taiwan, R.O.C.

Abstract- **From the resonance phenomena, we suggest that the blood pressure wave in the kidney is synchronized and the pressure wave front arrives at all the peripheral vascular beds (PVBs) inphase. The phase velocity of the blood pressure wave is very fast and its corresponding wavelength is far longer than the size of PVB of the kidney. Therefore, all the blood flows in PVB driven by the blood pressure wave will be kept inphase all around the kidney. To verify our inference, we used a Laser-Doppler flowmetry (LDF) to measure the renal cortical fluxes (RCF) at different sites on the kidney surface of dog and compare their frequency structures and phase differences with those of the abdominal aortic blood pressure (AABP). Using the averaged spectrum and the cross-covariance function, we conclude that the frequency structure of RCF is directly correlated with that of AABP and the RCF to AABP phase differences of all the five dogs are in a tiny range. The results strongly suggest that the pulsatile blood pressure wave is pushing the blood in PVBs and integrates all PVBs of the kidney as a unity as suggested by Huygens' principle.**

***Keywords*- Peripheral Vascular Bed, Huygens' Principle, Resonance, Inphase**

I. INTRODUCTION

How does the circulatory system distribute blood from the heart to the peripheral is a complex question. The heart, vascular structure, vascular wall elasticity, blood viscosity and many other hemodynamic properties are all playing the roles; numerous studies on this topic had been reported [1,2]. Before we go to any details of these parameters, the main theme has to be clarified; both the major players, the blood pressure and blood flow, were first to be considered and had been extensively investigated [1,2]. However, the mechanism of the blood distribution in the peripheral is not clear.

We will bring two important features in the circulation: First, the mean blood pressure keeps almost constant in the aorta, arteries, and even in small arteries, while it drops abruptly in the region where arterioles distribute numerous precapillary branches [3]. Second, the phase velocity of blood pressure wave increases from 3.5 m/sec in aorta to 14.3 m/sec in tibia artery and the stiffer peripheral vessels may accelerate the velocity even further; meanwhile, the blood flow velocity drops abruptly from 33 cm/sec in proximal ascending aorta to 0.6-31.7 mm/sec in arterioles [3,4]. They suggest that the potential energy is maintained in the artery system and that blood pressure wave can propagate from the aorta to the peripheral instantaneously.

To clarify the potential energy distribution in artery system, we proposed the resonance theory that is the natural radial oscillation due to the elasticity of vascular wall and deduced the blood pressure as the dominating player comparing to the blood flow in circulation [5,6,7]. According to the resonance theory, each organ or each elastic vascular bed may have its own natural frequency due to its wall elasticity; we had also studied the frequency properties of organs on pressure wave [5,7] and suggested that the elastic vascular bed of the kidney is one resonance unit to couple with aorta [5,7]. The renal artery becomes the relative small slit to synchronize the pressure wave that enters the kidney, while the peripheral vascular bed (PVB) in the kidney will encounter the wave front of this new wave source and therefore determine the blood flow; it is the Huygens' principle in physics. Thus, all blood flows in the PVBs driven by the same pressure wave front will succeed the frequency properties of the driving pressure wave and keep almost inphase anywhere around the organ.

In this study, basing on the conclusion of our previous works, we suggest that the PVBs of the whole kidney is unified by the long-wavelength pressure wave; therefore, at different sites of renal PVBs, their fluxes that is driven by the coupled blood pressure wave will continue the pulsatile properties generated by heart and keep approximately a constant phase.

II. METHODOLOGY

Animal Preparation and Experimental Setup

Five mongrel dogs of either sex, weighting from 7 to 14 Kg, were sedated with ketamine (10 mg/kg, im), anesthetized with Urethane (500mg/kg, iv). The dog was then placed on an operation table with a heated pad to keep the body temperature. Anesthesia was maintained by additional doses of anesthetics as required. The polyethylene tube (PE 240, Becton-Dickinson, USA) was inserted from the femoral artery into the abdominal aorta of the dog with a catheter-tip pressure transducer (P10EZ, Viggo-Spectramed, USA) to measure AABP.

Laser Doppler Flowmetry (MBF3, Moor Instruments Ltd., England) was used for the measurement; its time constant was set to 0.05 second and its cut-off frequency was 14.9 kHz. MBF3 samples the analogue signal with a 40Hz-sampling rate and then converts it into analogue output. An optical fiber probe (P10M+P17, plastic fiber 500μm O.D., Moor Instruments Ltd.) was calibrated by the calibration flux standard (Moor Instruments Ltd.) to ensure its stability and performance.

Experiments and Data acquisition

Before the surgery, the dog was put in a lateral position on the operation table. The left kidney was exposed from the dorsal side, and fixed with sterilized gauze sponges. The fatty capsule was separated carefully to avoid bleeding, and the surface of the kidney received an infusion of 37°C normal saline to keep it from drying during the experiments.

The optical fiber probe was gently touched vertically to the surface of the renal cortex to avoid artifacts introduced by respiration or other inner movements. The motion artifact

Report Documentation Page

Report Date	Report Type	Dates Covered (from... to)
25 Oct 2001	N/A	-

Title and Subtitle Estimation of Coherence Between the Pulsatile Aortic Blood Pressure and the Renal Cortical Flux in DODS	**Contract Number**
	Grant Number
	Program Element Number
Author(s)	**Project Number**
	Task Number
	Work Unit Number
Performing Organization Name(s) and Address(es) Biophysic Lab Institute of Physics Academia Sinica Taipei, Taiwan, R.O.C.	**Performing Organization Report Number**
Sponsoring/Monitoring Agency Name(s) and Address(es) US Army Research, Development & Standardization Group (UK) PSC 802 Box 15 FPO AE 09499-1500	**Sponsor/Monitor's Acronym(s)**
	Sponsor/Monitor's Report Number(s)

Distribution/Availability Statement
Approved for public release, distribution unlimited

Supplementary Notes
Papers from 23rd Annual International Conference of the IEEE Engineering in Medicine and Biology Society, October 25-28, 2001, held in Istanbul, Turkey. See also ADM001351 for entire conference on cd-rom.

Abstract

Subject Terms

Report Classification unclassified	**Classification of this page** unclassified
Classification of Abstract unclassified	**Limitation of Abstract** UU

Number of Pages
4

caused by the respiration can be easily detected; the period is about 3-5 times that of the heartbeat. Proper installation of the probe and good care of the animals during the experiments can reduce the artifact. Aortic blood pressure, both diastolic and systolic, was monitored during the experiments.

The RCF signal was recorded from the analogue output of MBF3. Both the AABP and RCF signals were connected to a simultaneous sample & hold card AX753 (AXIOM Technology Co., LTD. Taiwan, R.O.C.) and then to an A/D converter card AX5621 (AXIOM Technology) with 750Hz sampling rate. Both signals were sampled simultaneously and synchronously. There were 4-6 different sites on the surface of renal cortex measured within one hour to avoid physiological change in each dog; each site kept at least 1 cm apart the other and the positions were chosen where there are no visible vessels. In each measured site, we acquired 32 data sequences; each contains 4 second-long signals successively by a 486 PC. The data sequence recorded 6-14 pulses depending on the heart rates of the dogs.

Data analysis and Signal Process

On each site, we recorded a 64 second-long continuous signal. The period of each pulse was determined by the two lowest points of the blood pressure pulse. In each sequence, the mean and the coefficient of variance (CV = SD/mean) of the heart rates were calculated. Two criteria were employed to verify stable sequence to be averaged: (1) The CV of the heart rate of a sequence was under 10%. (2)The mean heart rate of one sequence varied within 2% of the mode of the mean heart rate measured in one site. The sequences that satisfied both criteria were selected.

The k-th selected sequence $x^{(k)}[n]$ was divided into a DC component and an AC component. The DC component $x_{DC}^{(k)}[n]$ was the mean value of the sequence. The AC component $x_{AC}^{(k)}[n]$ was thus equal to

$$x_{AC}^{(k)}[n] = x^{(k)}[n] - x_{DC}^{(k)}[n].$$

The AC component was then transformed with discrete Fourier Transform (DFT), and the spectrum was calculated as

$$\hat{X}_{per}^{(k)}[f] = \frac{1}{N}\left|\sum_{n=0}^{N-1} x_{AC}^{(k)}[n]\exp(-j2pfn)\right|,$$

where n was the nth sampling point and N represents the total sampling number in each sequence. In order to enhance the signal to noise ratio (SNR), an averaged spectrum

$$\hat{X}_{AVE}[f] = \frac{1}{P}\sum_{p=0}^{P-1} \hat{X}_{per}^{(k)}[f]$$

was employed, where a total of P selected sequences was averaged.

Besides the spectrum, we also evaluated the phase difference between RCF and AABP. Because RCF was too noisy, we used a biased cross-covariance function to estimate the mean phase difference [4,8]. For two periodic waves with the same periodicity, their cross-covariance function will be with the same periodicity. The maximum of each period of the biased cross-covariance function shows the two waves are inphase while the minimum of which implies those are out of phase. The mean phase difference between the two signals in each sequence was estimated by the phase lag between the zero lag and the lag of the maximum of the biased cross-covariance function as shown in Fig. 4.

All the signal processes were performed with MATLAB, IBM-PC version (Math Works, Natick, Mass., U.S.A.).

III. RESULTS

In each measurement, the blood pressure and the heart rate were monitored. The fundamental heart rates varied from dog to dog due to the size and strain. There were 24 measured sites; only 14 sites which had at least 10 sequences satisfied the criteria mentioned in the method and in which the heart rates in the range, 2.76±0.10 Hz, were selected. According to the mean blood pressure (MBP), the five dogs were classified into three physiological states: normal (MBP = 90-110 mmHg), slightly lower (MBP = 80-90mmHg) and lower (MBP = 60-80 mmHg).

The measurement of LDF reflects the relative change in tissue blood perfusion; the unit is therefore classifying as arbitrary units (AUs) depending on the method of calibration. We had developed an averaged spectrum to analyze RCF and their harmonics of heart rate [9].

The result of linear regressive analysis between the RCF frequency peaks and the harmonics of AABP is listed in table 1. Table 1A shows the result of the six selected sites of normal blood pressure, table 1B is the result of the six selected sites classified as lower blood pressure and table 1C demonstrates the result of all the selected sites. No matter what the MBP is, all the three tables show that a direct linear correlation between the six frequency peaks of RCF and the first six harmonics of AABP.

Table 1
The linear regressive analysis between RCF peaks and AABP peaks

A. For the selected sites classified as normal (n=6)

	Peak 1	Peak 2	Peak 3	Peak 4	Peak 5	Peak 6
Correlation Coeff.	1	0.96	0.97	0.97	0.95	0.98
Slope	1	0.99	1.00	1.00	1.02	1.01

B. For the selected sites classified as lower (n=6)

	Peak 1	Peak 2	Peak 3	Peak 4	Peak 5	Peak 6
Correlation Coeff.	1	1	0.98	0.96	0.99	0.97
Slope	1	1	1.01	1.00	1.03	1.01

C. For all selected sites (n=14)

	Peak 1	Peak 2	Peak 3	Peak 4	Peak 5	Peak 6
Correlation Coeff.	1	0.98	0.97	0.96	0.98	0.98
Slope	1	1.00	1.00	1.00	1.02	1.01

P<0.001, slope significantly different from zero slope

The RCF to AABP phase differences of the five dogs and their average estimated by the cross-covariance function is shown in figure 3; RCF lags AABP and the all keep in a tiny range relative to the range of the possible phase difference (360°) for each dog (mean±SD = 15.4±1.5, 45.4±4.8, 29.3±2.1, 39.6±0.5, 29.7±2.9 degrees; 2×SD / 360 = 0.8%, 2.5%, 1.2%, 0.3%, 1.6%; n = 3, 2, 4, 2, 3; for the five dogs,

respectively). Even among the five diverse dogs, their phase lags still gather in a small range (mean±SD = 31.9±11.5 degrees; 2×SD / 360 = 6.3%, n=5).

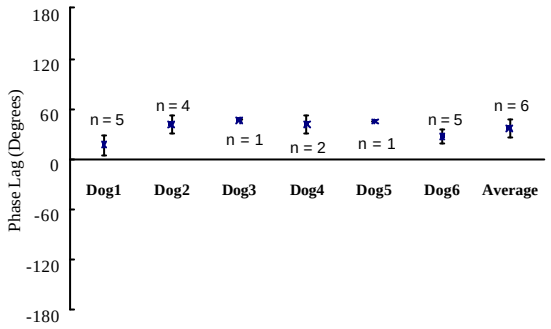

Figure 1: The RCF to AABP phase differences of the five dogs and their average estimated by the cross-covariance function

IV. DISCUSSION

In the last two decades, LDF is frequently used in the study of microcirculation [9]. The assessment between LDF and other methods frequently used in the microcirculation research had been published [10,11]; it is commonly accepted that LDF can follow both temporal variations of blood perfusion in a particular tissue and the spatial variations of perfusion among different regions of the same tissue. Although LDF can only reflect the relative change in tissue blood perfusion; however, using the detection of back scattering light, LDF can observe the solid organs such as kidney without a penetrate illumination and much preparation of the observed tissue. Thus, it is extensively used to measure the regional tissue blood perfusion in kidney [10].

Our data show that both AABP and RCF have the same periodicity and synchronize with each other (Table 2). It is also shown that, no matter what the MBP is normal or lower, RCF is synchronized with AABP as long as the pulsatility generated by the heart is regular. Because the only frequencies in a periodic wave are its harmonics, all frequencies except those of the harmonics of heartbeat have tiny energy and no importance in normal physiology state [4-7].

The blood pressure wave propagation implies the elastic energy transferring through the blood-filled vascular beds. The pressure wave will be coupled and redistributed according to the resonance and coupling [4,7]. The coupled pressure wave with long wavelength at the upstream of every PVB plays the role of a new "heart" to drive existing blood in vessels to flow, thus the forced flow should succeed the coupled pulsatility of the pressure wave and keep almost inphase around the whole resonance organ.

It had been reported that the mean transit time (MIT) of blood flow from the cat mesentery artery to its downstream arterioles measured by the microscopic indicator method is about 2 to 7.5 seconds (average value, 3.9 seconds, in 90 measurement) [2]. If the blood flow instead of blood pressure dominates the behavior in circulation, it can't be pulsatile and the phase differences in PVBs must be random. However, we found that not only the phase differences in different sites of the kidney of one dog but also those of the five diverse dogs are nearly inphase (Figure 3). These results strongly support our inference that the blood pressure wave integrates all PVBs of the kidney as one unit and drives the blood within the PVBs.

Many other slowly periodic fluctuations in renal hemodynamics had been reviewed [12]. The spontaneous oscillation frequency of tubuloglomerular feedback (TGF) ranges from 20-50 mHz in rats [4] and the vasomotion is about 120-180 mHz [13,14]. The driving forces of those fluctuations are originated from the local tissue and act as the feedback compensation response to the physiological changes; their responses are slow and may exist only in some specific physiological condition. This is similar to the blood pressure wave in the arteries where we can observe the respiratory wave mixed with the pulsatile blood pressure; however, one can extract the respiration wave from the pulsatile blood pressure wave through suitable analysis. The pulsatile wave is the fundamental carry wave; the slow fluctuations can modulate the amplitude, but cannot change the frequency. Furthermore, these slow fluctuations are not in the window of our studies.

V. CONCLUSION

In summary, this study demonstrates that RCF succeeds the pulsatility generated by the heart and the phase differences between RCF to AABP at different sites of the kidney are almost the same in the same dog and even in different dogs. These findings suggest that the pulsatile blood pressure wave is pushing the blood in PVBs and integrates all PVBs of the kidney as a unity as suggested by Huygens' principle.

REFERENCES

[1] W.R. Milnor, *Hemodynamics, 2nd. Ed.,* Williams & Wikins: Baltimore, MD, 1989.

[2] S.H. Nellis and Lee J.S., "Dispersion of indicator measured from microvessels of cat mesentery," *Cir. Res.*, vol.35, pp. 580-591, 1974.

[3] W.W. Nichols and M. F. O'Rourke, *McDonald's blood flow in arteries, 3rd. ed.*, Edward Arnold: London:, 1990.

[4] M. Intaglietta, W.R. Tompkins, and D.R. Richardson, "Velocity measurement in the microvasculature of the cat omentum by on-line method," *Microvasc. Res.,* Vol. 2, pp. 462-473, 1970.

[5] Y.Y. Wang Lin, S.L. Chang, Y.E. Wu, T.L. Hsu, and W.K. Wang, "Resonance, the missing phenomenon in hemodynamics," *Cir. Res.*, Vol. 69, pp. 246-249, 1991.

[6] Y.Y. Wang Lin, C.C. Chang, J.C. Chen, T.L. Hsu, and W.K. Wang, "Pressure wave propagation in a simplified artery with large radial dilation," *IEEE Engineering Med. & Biol. Magazine.*, Vol.16(1), pp. 51-56, 1997.

[7] G.L. Yu, Y.Y. Wang Lin, and W. K. Wang, "Resonance in the kidney system of rats," *Am. J. Physiol*. Vol. 267 *(Heart Circ. Physiol*. Vol, 36), pp. H1544-H1548, 1994.

[8] R. E. Challis and R.I. Kithy, "Biomedical signal processing, part 1: time-domain methods," *Med. & Biol. Eng. & Comput*., Vol. 28, pp.509-524, 1990.

[9] M.Y. Jan, H. Hsiu, T.T. Hsu, Y.Y. Wang Lin and W.K. Wang, "Measurement and analysis of the pulsatile renal cortical fluxes in rats with a fast Laser-Doppler flowmetry," Biomed. Eng. Appl. Basis. Comm., vol. 12, pp.60-65, 2000.
[10] R.J. Roman, "Renal blood flow," in: Laser-Doppler flowmetry. A.P. Shepherd and P.A. Oberg, Eds, Kluwer Academic Publisher: Norwell, 1989, pp.289-304.
[11] K. Tyml and C.G. Ellis, "Simultaneous assessment of red cell perfusion in skeletal muscle by Laser-Doppler flowmetry and video microscopy," *Int. J. Microcirc.: Clin. Exp*., Vol. 4, pp.397-406, 1985.
[12] N.H. Holstein-Rathlou and D.J. Marsh, "Renal blood flow regulation and arterial pressure fluctuation: a case study in nonlinear dynamics," *Physiol. Rev.* Vol. 74(3), pp. 637-681, 1994.
[13] D. Casellas and L.C. Moore. "Autoregulation and tubuloglomerular feedback in jutagmedullary glomerular arterioles," *Am. J. Physiol*. Vol. 258 (*Renal Fluid Electrolyte Physiol*. Vol. 27), pp. F660-F669, 1990.
[14] J.V. Meyer, L. Lindbom, and M. Intaglietta, "Coordinated diameter oscillations at arteriolar bifurcations in skeletal muscle," *Am. J. Physiol*. Vol. 253, pp. H568-H573, 1987.